

Improvement of Metabolic Parameters Resulted from Levothyroxine Therapy in Hypothyroid Type 2 Diabetes Mellitus Patient

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Figure 1. Patient's profile shows obesity and diffuse goiter in her neck

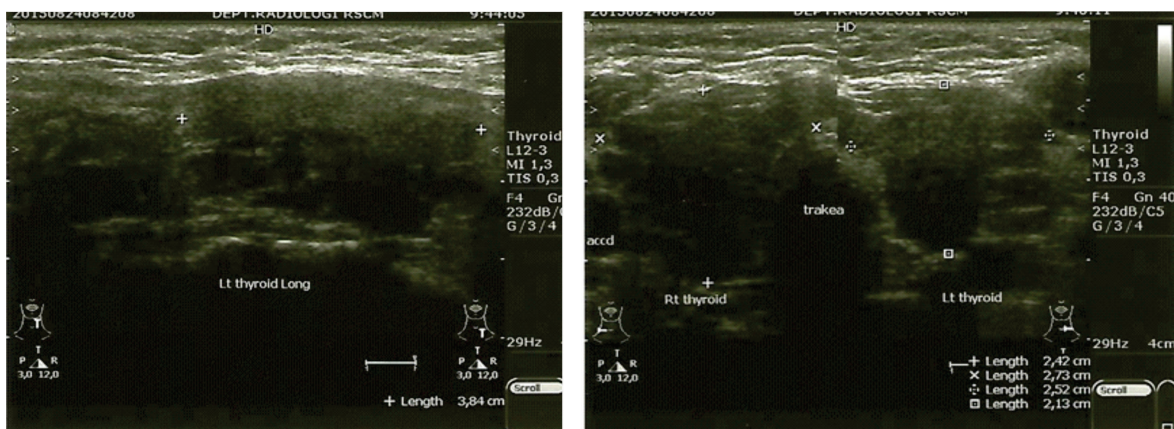


Figure 2. Thyroid ultrasound shows diffuse goiter

Association between diabetes and thyroid dysfunction has been recognized since long time ago.¹ Prevalence of thyroid dysfunction is higher in type 2 diabetes population compared to normal population.¹⁻³ A meta-analysis by Han C⁴ obtained the pool adjusted prevalence of subclinical hypothyroidism around 10.2% among type 2 diabetes patients. This meta-analysis use 36 studies around the world with the range prevalence from 4.69-18.86%.⁴ This phenomenon is very interesting in endocrinology field since several risk factors may contribute to hypothyroidism in type 2 diabetes patients, such as advanced age, female gender, poor glycemic control, metabolic syndrome, family history of thyroid diseases, and the use of metformin.⁵⁻¹⁰

As thyroid hormone has an important roles in body metabolism, hypothyroidism is usually accompanied by several metabolic parameters which can be improved as the patient has thyroxin substitution therapy.¹¹ These metabolic conditions include dyslipidemia, poor glycemic control, and obesity. Therefore, assessment of thyroid function is an integral part of comprehensive management of type 2 diabetes mellitus patients, especially with obesity, dyslipidemia, and metabolic syndrome. It is also recommended by American Thyroid Association (ATA),¹² European Thyroid Association (ETA),¹³ and British Thyroid Foundation.¹⁴

This is a case of 51 year-old woman with uncontrolled type 2 diabetes mellitus which was diagnosed 1.5 year earlier, obesity with body mass index 32.2 kg/m², waist circumference of 113 cm, diffuse goiter with neck circumference 40 cm, and hypertension with blood pressure >140/90 mmHg. Since 6 months ago, she often seemed like having less concentration or daydreaming, chronic fatigue, depression, and low food intake. Her body weight had been increasing over time. Her hypothyroidism clinical scoring Billewicz and Zulewski criterias were 17 and 8 respectively, showing that she tended to experience hypothyroidism. From laboratory examination, fasting blood glucose was 216 mg/dL and 2-hour postprandial blood glucose was 320 mg/dL with level of HbA1c was 9.9%, triglyceride level was 486 mg/dL, HDL cholesterol 46 mg/dL, LDL cholesterol 157 mg/

dL, and total cholesterol was 269 mg/dL. Thyroid ultrasound showed a diffuse goiter in both lobes of her thyroid gland.

Thyroid function examination was performed and the result was subclinical hypothyroidism with TSHs 74.83 mIU/L (normal 0.27-4.2 mIU/L) and free-T4 1.02 µg/L (normal 0.93-1.70 µg/L). She was diagnosed as having uncontrolled type 2 diabetes mellitus with metabolic syndrome, obesity, and severe hypertriglyceridemia, and subclinical hypothyroidism based on laboratory examination. Although hypothyroidism is actually at the clinical stage and based on clinical presentation. She was treated with analogue rapid-acting insulin (aspart) 12 unit three-times daily and analogue long-acting insulin (glargine) 14 unit once daily, which was the same dose of insulin she took before. According to European Thyroid Association (ETA) Guideline for subclinical hypothyroidism,¹³ she had been given levothyroxin 100 µg once daily.

After one month therapy of thyroxin, symptoms were getting better such as more active physically, less symptoms of depression, reduced weight with the same insulin dose. The TSHs level decreased to 29.15 mIU/L. After three months of thyroxin therapy, hypothyroidism symptoms are reduced with Billewicz score and Zulewski score 7 and 5 respectively. Body mass index reduced to 31.5 kg/m², waist circumference 106 cm, neck circumference 37 cm, and normal blood pressure. HbA1c level decreased to 9% with same insulin dose, triglyceride 223 mg/dL, HDL cholesterol 54 mg/dL, LDL cholesterol 145 mg/dL, and total cholesterol 255 mg/dL. Clinical and laboratory metabolic parameters were improved, although patient had not regular exercise and insulin dose were remain steady. Her TSHs level decreased to 13.19 mIU/L after three months of thyroxine therapy.

After six months therapy of levothyroxin, the clinical presentation resolved; no depression symptoms, more active physically, and decreased body mass index. Her TSHs level is 5.81 mIU/L with free-T4 1.55 µg/L, HbA1c 7.8% (fasting blood glucose 162 mg/dL and 2-hour postprandial blood glucose 155 mg/dL with the same insulin dose, triglyceride 176 mg/dL, HDL cholesterol 48 mg/dL, LDL cholesterol 106 mg/

dL, and total cholesterol 173 mg/dL.

Hypothyroidism in type 2 diabetes mellitus patient can worsen morbidities such as obesity and dyslipidemia, which contribute to more complications, mortality risk, and decrease quality of life.¹⁵ Routine screening of thyroid function in type 2 diabetes mellitus patients still controversial nowadays. Not all endocrine and diabetes societies mention thyroid function in the list of diabetes panel examination like lipid profiles, kidney function, microalbuminuria, and electrocardiography. In the other hand, several thyroid societies all over the world insert type 2 diabetes mellitus as a condition which thyroid function test suggested to be examined.¹²⁻¹⁴ Therefore, screening of thyroid function in diabetes patient must be right on target. If the patient's clinical presentation has a tendency to develop hypothyroidism, such as obesity, metabolic syndrome, poor glycemic control, goiter, low activity, slow movement, bradycardia, chronic fatigue, examination of thyroid function is mandatory.

The patient in this medical illustration is a good example of thyroxin treatment which can improve several metabolic parameters. Gluvic Z et al¹¹ and Kumar A et al¹⁶ reported significant metabolic effects of thyroxin replacement therapy in hypothyroid patients will improve metabolic syndrome and atherosclerosis. This contributes to reduced cardiovascular risk in diabetes population, as they are already have higher risk of cardiovascular events.¹¹ In our patient, as the TSH level decreased gradually, the HbA1c, lipid profiles, fasting blood glucose and 2-hour post-prandial blood glucose, body mass index, waist circumference, neck circumference had also been reduced. More studies are needed to investigate the hard endpoint such as major cardiovascular event and mortality.

REFERENCES

- Palma CCSSV, Pavesi M, Nogueira VG, et al. Prevalence of thyroid dysfunction in patients with diabetes mellitus. *Diabetol Metabol Syndr*. 2013;58(5):1-5.
- Mouradian M, Abourizk N. Diabetes mellitus and thyroid disease. *Diab Care*. 1983;6(5):512-20.
- Johnson JL. Diabetes control in thyroid disease. *Diabetes Spectrum*. 2006;19(3):148-53.
- Han C, He X, Xia X, et al. Subclinical hypothyroidism and type 2 diabetes: a systematic review and meta-analysis. *PloS One*. 2015;10(8):1-22.
- Demitrost L, Ranabir S. Thyroid dysfunction in type 2 diabetes mellitus: a retrospective study. *Indian J Endocr Metab*. 2012;16:S334-5.
- Al-Geffari M, Ahmad NA, Al-Sharqawi AH, Youssef AM, Al-Naqeb D, Al-Rubeaan K. Risk factors for thyroid dysfunction among type 2 diabetic patients in a highly diabetes mellitus prevalent society. *Int J Endocrinol*. 2013;ID 417920:1-6.
- Alam MJ, Mukti MNM, Hoque MM, et al. Cross-sectional evaluation of thyroid hormone levels in non-diabetic and diabetic patients in Bangladeshi population. *Asian J Biol Sci*. 2013;6(4):228-33.
- Shashi A, Devi U, Singla S. Association between hypothyroidism and metabolic syndrome in type 2 diabetic patients: a cross-sectional study. *Int J Basic App Med Sci*. 2013;3(1):98-109.
- Guney E, Efe B, Akalin A, Kebapci N, Erenogiu E. Thyroid disease in diabetes mellitus. *Turkish J Endocr Med*. 1999;3:119-22.
- Diez JJ, Igleas P. Relationship between serum thyrotropin concentrations and metformin therapy in euthyroid patients with type 2 diabetes. *Clin Endocrinol*. 2013;78:505-11.
- Gluvic Z, Sudar E, Tica J, et al. Effects of levothyroxine replacement therapy on parameters of metabolic syndrome and atherosclerosis in hypothyroid patients: a prospective pilot study. *Int J Endocrinol*. 2015;ID147070:1-9.
- Garber JR, Cobin RH, Gharib H, et al. Clinical practice guidelines for hypothyroidism in adults: cosponsored by the American Association of Clinical Endocrinologists and the American Thyroid Association. *Endocr Pract*. 2012;18(6):988-1028.
- Pearce SHS, Brabant G, Duntas LH, et al. 2013 ETA guideline: Management of subclinical hypothyroidism. *Eur Thyroid J*. 2013;2:215-28.
- Beastall GH, Beckett GJ, Franklyn J, et al. United Kingdom guidelines for the use of thyroid function tests. British Thyroid Association, British Thyroid Foundation, and The Association for Clinical Biochemistry, 2006.
- Brenta G. Diabetes and thyroid disorders. *Br J Diabetes Vasc Dis*. 2010;10:172-7.
- Kumar A. The effect of L-thyroxine on metabolic parameters in newly diagnosed primary hypothyroidism. *Clin Exp Pharmacol*. 2013;3(3):1-4.